

What is transdiagnostic, immune-stratified precision psychiatry?

Transdiagnostic, Immune-Stratified Precision Psychiatry: What It Means

This concept combines three ideas: going beyond traditional diagnoses (transdiagnostic), using immune biology to define subgroups (immune-stratified), and tailoring care accordingly (precision/stratified psychiatry).

Transdiagnostic Perspective

- A transdiagnostic approach **cuts across DSM/ICD categories**, grouping people by shared mechanisms or symptom dimensions instead of fixed labels like depression vs schizophrenia (Qiu et al., 2024; Williams et al., 2023; McGorry et al., 2018).
- Inflammation, circadian disruption, and microbiome changes are examples of **transdiagnostic mechanisms** seen in multiple disorders (Comai et al., 2025; Yuan et al., 2019; Williams et al., 2023).

Immune-Stratified: Using Immune Biology to Define Subtypes

- Patients are clustered into subgroups based on immune markers: cytokines, blood cell ratios, DNA methylation of immune genes, or multi-omics immune profiles.
- Examples:
 - An **immuno-inflammatory biotype** across major psychiatric disorders, defined by methylation of adaptive/innate immunity genes, elevated neutrophils, low lymphocytes, and specific brain connectivity patterns; this group responds worse to standard treatments (Tang et al., 2025).
 - In depression, **immune-related clusters** with higher BMI, more severe symptoms, and elevated CRP, IL-1RA, and CCL2 vs low-inflammation clusters with different brain and ECG features (Hagenberg et al., 2024).
 - Trauma-exposed patients across diagnoses show a **pro-inflammatory profile**, with IL-6 mediating the link between childhood maltreatment and adult psychiatric illness (Van Den Noortgate et al., 2025).

Examples of Immune-Defined Clusters

Basis of stratification	What differs	Citations
Immune DNA methylation + fMRI	Brain connectivity, blood counts, treatment response	(Tang et al., 2025)
Plasma cytokines + PBMC RNA-seq	Symptom severity, BMI, ventricles, ECG	(Hagenberg et al., 2024)
Trauma history + cytokines	IL-6, broader pro-inflammatory markers	(Van Den Noortgate et al., 2025)

FIGURE 1 Different ways immune data define psychiatric subtypes.

Precision / Stratified Psychiatry Angle

- **Precision psychiatry** aims to integrate biomarkers, imaging, genetics, and clinical data to select the right treatment for each person, moving beyond “one-size-fits-all” (Comai et al., 2025; Miller et al., 2025; Arns et al., 2021; Williams et al., 2023).
- **Stratified psychiatry** is a pragmatic step: using biomarkers to assign patients to subgroups that are more likely to benefit from specific **existing (on-label)** treatments (Arns et al., 2021).
- Immunopsychiatry provides a template: enrich anti-inflammatory trials for patients with elevated immune markers, use outcomes that map to immune-linked symptoms, and verify target engagement (Miller et al., 2025; Drevets et al., 2022).

Putting It Together

Transdiagnostic, immune-stratified precision psychiatry means:

1. ignoring rigid disorder boundaries;
2. defining biologically coherent subgroups using immune signatures; and
3. using those subgroups to guide prognosis and match patients to mechanism-based (often anti-inflammatory) or optimized existing treatments.

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